REMARKS

In the above-identified application, claims 71-161 were pending prior to entry of the present amendment. The present amendment adds claims 162-189; amends claims 71, 72, 95, 114, 115, 149 and 150, in part, for clarity; and cancels claims 75 and 118, without prejudice. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any subject matter of the claims as previously presented.

Applicants have amended the claims, in part, for clarity. In particular, claims 71, 72 have been amended to recite a method to positively identify cells; claim 95 has been amended to recite cells that are positively identified; and claim 150 has been amended to recite a kit for the positive identification of cells. Support for these amendments to claims can be found at least at page 5, lines 18-21 where is it disclosed that one aspect of the invention is a method to label cells with a product and at page 10, lines 6-11 where it is disclosed that products which can be identified are products secreted by the cells. Support for the recitation of "positively identified" can also be found at least at page 9, lines 33-35, that discloses that the captured product permits the cells to be detected, i.e., identified, and sorted, that is separated. Support for the amendment to claims 71, 72 and 115 that recites that the cells are not lysed by the methods can be found at least at page 5, lines 8-10. Support for the amendment to claims 114, 115 and 149 that recites positively separating, positively separate, or positively separated, respectively, is inherent in the disclosure found at least at page 4, lines 15-17, where it is disclosed that the separation is based on the products secreted by the cells, that is, positive separation based on secreted products. Support can also be found at least at page 9, lines 33-35, that disclose that the captured product permits the cells to be sorted, that is separated.

Support for claim 162 can be found at least at page 26, lines 20-30. Support for claims 163-164 can be found at least at page 12, lines 21-27 and at page 15, lines 11-14. Support for claim 165 amendment can be found at least at page 10, lines 12-14. Support for claim 166 can be found at least at page 15, lines 11-14.

Support for claims 167-171 can be found at least at page 5, lines 25 through page 6, line 19. Support for claims 172-189 can be found throughout the specification and in particular at least at page 4, lines 15-31; page 9, lines 32-34 and page 10, lines 1-11.

Attached hereto is a marked up version of the changes to the claims by the current amendment with additions underlined and deletions bracketed. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**".

I. Interview

Applicants thank the Examiner for the courtesy of an interview on November 29, 2000, where pending prior art rejections were discussed.

II. Election of Species

In the above-identified application, a Restriction Requirement was mailed on February 14, 2001. Claims 112, 113, 145, and 146 are withdrawn by the Examiner as being directed to a non-elected invention. Applicants expressly reserve his/her right under 35 U.S.C. § 121 to file a divisional application directed to the non-elected subject matter during the pendency of this application, or an application claiming priority from this application.

The Examiner also required an election of species.

1. between the species in claim 77 (wherein the label moiety is fluorochromated) and the species in claims 78 and 79 (wherein the label moiety is magnetizable);

2. between the species in claim 82 (wherein the anchor moiety is a lipid) and the species in claim 83 (wherein the label moiety is an antibody);

3. among the species in claim 86. If the species "cytokines" is elected then Applicants are required to elect among the species of cytokines in claim 87;

4. among the species in claim 89;

5. among the species in claim 91;

6. between the species in claim 99 (wherein the anchor moiety is a lipid) and the species in claim 100 (wherein the label moiety is an antibody);

7. between the species of claim 102 (wherein the label moiety is fluorochromated) and the species of claim 103, (wherein the label moiety is magnetizable);

8. among the species in claim 104. If the species "cytokines" is elected then Applicants are required to elect among the species of cytokines in claim 105;

9. among the species in claims 107 and 108;

10. among the species in claim 111; and

11. with the methods and kits of claims 115-144, and 150-161 being subject to the same species election requirement as in items 1-10 above.

For item 1 above, Applicants elect species fluorochromated (claim 77);

For item 2 above, Applicants elect species antibody (claim 83);

For item 3 above, Applicants elect species cytokine (claim 86) and the cytokine "IFNγ" from claim 87;

For item 4 above, Applicants elect species dextran molecules (claim 89);

For item 5 above, Applicants elect species CD45 (claim 91);

For item 6 above, Applicants elect species antibody (claim 100);

For item 7 above, Applicants elect species fluorochromated (claim 102);

For item 8 above, Applicants elect species cytokine (claim 104) and the cytokine "IFNγ" from claim 105;

For item 9 above Applicants elect species CD45;

For item 10 above, Applicants elect species dextran molecules; and

For item 11 above that relates to election of species from methods and kits, Applicants elect the same species as in items 1-10 above, that is, fluorochromated, antibody, cytokine (IFNγ), dextran and CD45.

III. Response to outstanding rejections from Advisory Action mailed March 17, 2000.

a)Rejection of claims under Section 112, first paragraph

In the Advisory Action mailed March 17, 2000, the Examiner maintained the rejection of claims under Section 112, first paragraph. The Examiner alleged that the specification is enabling for methods and kits which use a high viscosity or gel forming medium.

Applicants traverse this rejection and maintain their position that the specification is enabling over the full scope of the pending claims. In order to satisfy the requirements of 35 U.S.C. § 112, first paragraph, a patent application must teach one of ordinary skill in the art how to make and use the claimed invention. Applicants have fulfilled this requirement.

Applicants submit that the present invention encompasses a variety of methods for positively identifying cells secreting a product and a variety of methods for positively separating cells labeled with a product. The specification discloses a variety of incubation conditions for the methods. In particular, see the specification at page 10, lines 12-34 which discloses anchoring moieties; page 11, lines 3-14 and lines 21-29 which discloses capture moieties and pages 12-15 which discloses coupling mechanisms. Additionally, the specification at page 17, lines 6-29 discloses a variety of incubation conditions that affect the methods, such as incubation time, incubation medium, cell concentration and the level of secretion of the product. Additionally, the examples provide illustrative methods for positively identifying cells that are labeled with a secreted product. In particular, experiments described in Example 1, the results of which are shown in Figure 6b of the specification as originally filed, demonstrate that successful identification of cells labeled with a product was achieved without the use of high viscosity medium.

Applicants submit concurrently herewith the Declaration of Dr. Mario Assenmacher (Assenmacher Declaration). Paragraph 4 of the Assenmacher Declaration describes incubation conditions that influence the methods to positively separate product-producing cells. Assenmacher Declaration, Paragraph 4 , states that the methods can be performed in incubation medium that does not contain a substance which slows diffusion. Optionally, the incubation medium may include a substance that slows diffusion, depending upon the incubation conditions used. As concluded by the Assenmacher Declaration, methods to positively identify cells and to positively separate cells can be successfully performed in the absence of high viscosity or gel forming medium.

With respect to claims that recite kits, the Advisory Action maintained the rejection of claims that recite kits and that do not recite as an ingredient, a substance that slow diffusion. See Advisory Action mailed March 17, 2000, page 2, paragraph 3. Applicants submit that since the methods of identifying cells with a product secreted by the cells or methods of positively separating cells labeled with a product can be performed in the presence or absence of a substance which slows diffusion, depending upon incubation conditions, this rejection of claims that recite kits must fail.

Therefore, Applicants submit that the Section 112, first paragraph rejection of claims based on the requirement for the presence of a high viscosity or gel forming medium must fail. Applicants respectfully request a withdrawal of the Section 112, first paragraph rejection of claims.

b) Rejection of claims under Section 102(b) over Kohler et al.

In the Advisory Action mailed March 17, 2000, the rejection of claims under Section 102(b) was maintained over Kohler et al.

Applicants traverse this rejection of claims and submit that the presently claimed invention is novel over Kohler et al. Pending claims 71 and 72 recite a method to positively identify cells and claim 95 recites that the cells are positively identified. Pending claims 114 and 115 recite a method to positively separate cells and 149 recites that the cells are positively

separated. Pending claims 71, 72, 95, 114, 115, and 149 all recite that the product is labeled. Additionally, pending claims 71, 72 and 115 recite that the cells are not lysed by the methods.

In contrast, Kohler et al. discloses a method to negatively select cells, that is, cells having trinitrophenyl (TNP) coupled to their surface are lysed in the presence of a cytotoxic complement upon secretion of wild-type antibody and binding of antibody to TNP, while cells that do not produce antibody or produce mutant antibody preferentially survive.

Thus, each and every element of the claimed invention is not disclosed by Kohler et al. and the rejection must fail as a matter of law. Applicants request withdrawal of this Section 102(b) rejection of claims as it applies to new claims.

c) Rejection of claims under Section 103 over Kohler et al. in view of Hunt and Segal (U.S. Pat. No. 4,676,980)

In the Advisory Action mailed March 17, 2000, the rejection of claims under Section 103 was maintained over Kohler et al. in view of Hunt and Segal.

Applicants traverse this rejection of claims. In order to establish a *prima facie* case of obviousness, there has to be some motivation or suggestion provided by the references, or in combination with the knowledge available to the skilled artisan, to modify the art cited or to combine reference teachings. The cited references must also provide a reasonable expectation of success. There is no suggestion in any of the cited references to combine Kohler with Hunt and Segal and if combined, one of skill in the art would not arrive at the presently claimed invention. Applicants submit that the combination of references cited does not provide motivation for or a reasonable expectation of successfully arriving at the claimed invention.

Pending claims 71 and 72 recite methods for positively identifying cells, wherein the cells are not lysed by the method and claim 95 recites cells positively identified based on a product secreted by the cells, wherein the product is labeled with a label moiety. Kohler does not suggest identifying cells labeled with a product (wherein said product is labeled with a label moiety) because in Kohler et al., the cells producing product, IgM, that is bound to the TNP are lysed upon binding with complement. Pending claims 114 and 115 recite a method to positively

separate cells and 149 recites that the cells are positively separated. Kohler et al. suggest a method for the negative selection of cells and does not suggest the presently claimed invention. In Kohler et al., cells secreting wild-type antibody, which binds to TNP coupled to the cell surface, are lysed and the desired cell population is the population of cells that preferentially survives. In Kohler et al. the cells that secrete wild-type product cannot be positively separated and, for example, subjected to a further round of culturing and separation because in Kohler et al. the cells secreting wild-type product are lysed.

With respect to claims that recite kits, the Advisory Action mailed March 17, 2000, maintained the Section 103 rejection of claims that recite kits. Applicants traverse this rejection. Applicants have amended claim 150 to recite a kit for the positive identification of cells that comprises at least one of an anchoring moiety and a capture moiety. New claim 162 recites that the kit comprises a product capture system; new claim 163 recites that the anchor moiety is prepared for coupling to the capture moiety; new claim 164 recites that the capture moiety is prepared for coupling to the anchor moiety; and new claim 165 recites that the anchor moiety is coupled to the capture moiety. Kohler et al., discloses a method for the negative selection of cells. Kohler et al., taken alone or in combination with Hunt and Segal, does not suggest a kit for use in the positive identification of cells as is presently claimed.

Applicants submit that the present invention is non-obvious in view of the cited references and respectfully request withdrawal of the Section 103 rejection as it applies to new claims.

CONCLUSION

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Acc unt No. 03-1952** referencing docket no. 212302000320. However,

the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: May 24, 2002 By: _____

Randolph Ted Apple
Registration No. 36,429

Morrison & Foerster LLP
755 Page Mill Road
Palo Alto, California 94304-1018
Telephone: (650) 813-5933
Facsimile: (650) 494-0792

VERSION WITH MARKINGS TO SHOW CHANGES MADE

DIRECT SELECTION OF CELLS BY SECRETION PRODUCT

In the claims

Claims 75 and 118 have been cancelled, without prejudice.

New claims 162-189 have been added.

Claims 71, 72, 95, 114, 115, 149 and 150 have been amended as follows:

71. (Once amended) A method to positively identify [label] cells [with] based on a product secreted by the cells, comprising culturing said cells under conditions wherein the product is secreted and bound to a capture moiety coupled to said cells wherein said capture moiety specifically binds the product, thereby labeling cells with said product, and wherein said product is [has been] labeled with a label moiety, and wherein said cells are not lysed during said method.

72. (Once amended) A method to positively identify [label] cells [with] based on a product secreted by the cells, comprising the steps of:

a) coupling said cells to a capture moiety;

b) culturing said cells under conditions wherein the product is secreted and bound to said capture moiety, thereby labeling cells with a product secreted by said cells; and

c) labeling said product with a label moiety, and wherein said cells are not lysed during said method .

95. (Once amended) A composition comprising cells positively identified [labeled by] based on a product secreted by said cells, wherein said cells are coupled to a capture moiety,

wherein said product secreted by said cells is bound to said capture moiety [specifically binds the product secreted by said cell], and wherein said product is labeled with a label moiety.

114. (Once amended) The method of claim 71 further comprising the step of positively separating said cells labeled with said product secreted by said cells, wherein said product is labeled with a label moiety.

115. (Once amended) A method to positively separate cells based on a product secreted by the cells, comprising the steps of:

a) culturing cells coupled to a capture moiety under conditions wherein a product is secreted, wherein said product secreted by said cells [is] specifically binds [bound] to said capture moiety, thereby producing cells labeled with said product wherein said cells are not lysed by said method, and wherein said product is labeled with a label moiety; and

b) positively separating said cells labeled with said product.

149. (Once amended) A composition comprising cells positively separated based on a product secreted by the cells, wherein said cells are coupled to a capture moiety and said product secreted by said cells is specifically bound to said capture moiety and wherein said product is labeled with a label moiety.

150. (Once amended) A kit for the positive identification [detection] of cells that secrete a product, comprising:

a) at least one of an anchoring moiety and a capture moiety;

b) a label moiety for detecting captured product; and

c) instructions for use of the reagents, all packaged in appropriate containers.